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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/692,401	10/19/2000	Leonora Heidecker	L0461/7097-(JRV)	7318

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EXAMINER	
VANDERVEGT, FRANCOIS P	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 12/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/692,401	HEIDECKER ET AL.	
	Examiner	Art Unit	
	F. Pierre VanderVegt	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 July 2003 and 08 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,7,8,10,16,18-20,34,40-44,46,52,53 and 58-77* is/are pending in the application.

4a) Of the above claim(s) *10,16,18-20,34,40,41,44,46,52 and 53* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7,8,42,43 and 58-77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The Examiner in charge of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to F. Pierre VanderVegt, Ph.D. in Art Unit 1644.

This application claims the benefit of the filing date of provisional applications 60/160,374 and 60/179,570.

Claims 5-6, 9, 11-15, 17, 21-33, 35-39, 45, 47-51 and 54-57 have been canceled.

Claims 1-4, 7-8, 10, 16, 18-20, 34, 40-44, 46, 52-53and 58-77 are currently pending.

Claims 10, 16, 18-20, 34, 40-41, 44, 46 and 52-53 stand as withdrawn.

Claims 1-4, 7-8, 42-43 and 58-77 are the subject of examination in the present Office Action.

1. Applicant's arguments with respect to claims 1-4, 7-8, 42-43, and 58- 77 in the amendment filed September 8, 2003 and the remarks filed July 14, 2003 have been considered but are moot in view of the new ground(s) of rejection. In view of the new grounds of rejection, this Office Action is made NON-FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-4, 7-8, 42-43, and 58- 77 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was

in possession of the claimed genus. (See Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, especially page 1106 3rd column). A "representative number of species" means that the species that are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. MPEP 2163 II.A.3a.ii.

Claims 1-3 broadly recite functional variants of the MAGE-A3 HLA class II-binding peptides defined by SEQ ID NOs: 4, 5 and 6, all of which share the common core sequence RIGHLYIL (SEQ ID NO: 6), including variants comprising an amino acid deletion, addition or substitution. Claim 4 broadly encompasses an isolated MAGE-A12 class I binding peptide which binds HLA Cw*07 and consists of a functional variant of a fragment of SEQ ID NO: 2 comprising an amino acid addition, deletion or substitution. Thus Applicant has disclosed only a limited number of variants. The specification does not disclose the ability of any of these peptides to bind to any other HLA class I molecule other than Cw*07, nor does the specification disclose any variants comprising sequence changes within or adjacent to the core sequence that can bind to Cw*07. The specification also does not disclose which residues of the core sequence are required for binding, i.e., cannot be changed and maintain functional HLA class I binding, nor does it disclose where within that core sequence amino acid residues can be added, which residues can be changed or deleted or what type of change can actually be tolerated. It does not appear based upon the limited disclosure that Applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the limited number of species disclosed and the extensive variation permitted within the genus of "MAGE-A3 HLA class I-binding peptides."

Consequently, Applicant was not in possession of the instant claimed invention. See Regents of the University of California v. Eli Lilly and Co. 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). Adequate written description of genetic material "'requires a precise definition, such as by structure, formula, chemical name, or physical properties,' not a mere wish or plan for obtaining the claimed chemical invention." Id. 43 USPQ2d at 1404 (quoting Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606). The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter of the claim. Id. 43 USPQ2d at 1406. A description of what the genetic material does, rather than of what it is, does not suffice. Id.

While the instant claims are drawn to peptides and not to nucleic acids, the cited case law is relevant because there is limited disclosure of the structure, formula, or physical properties of a

"functional variant" and there is only a disclosure of what the "functional variant" does (bind Cw*07), rather than of what it is.

3. Claims 1-4, 7-8, 42-43, and 58- 77 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated MAGE-A12 class I binding peptide which binds HLA Cw*07, wherein said peptide consists of a fragment of the amino acid sequence of SEQ ID NO:2, and wherein said fragment comprises SEQ ID NO:4, 5, or 6, does not reasonably provide enablement for an isolated MAGE-A12 class I binding peptide which binds HLA Cw*07, wherein said peptide consists of a functional variant of a fragment of SEQ ID NO:2 or a functional variant of SEQ ID NO: 4, 5 or 6 comprising an amino acid addition, deletion or substitution. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1, 2 and 3 most broadly encompass a MAGE-A12 peptide that consists essentially of the peptide of SEQ ID NO: 4, 5 or 6 which bind to a Class I-C HLA molecule. Claim 4 broadly encompasses an isolated MAGE-A12 class I binding peptide that binds HLA Cw*07 and consists of a functional variant of a fragment of SEQ ID NO: 2 comprising an amino acid addition, deletion or substitution.

The specification does not identify the residues of the peptides that are important for interaction with the HLA class I molecule or with the responding T cell and therefore provides no guidance in regard to the residues that are especially recalcitrant to change and maintain the functional nature of the peptide. Further, there is no disclosure of the non-interaction residues that are not amenable to change. Applicant's contention in the remarks filed July 14, 2003 that preferred interaction residues for HLA-C haplotype binding is acknowledged (remarks page 8), however there are differences in the actual binding residues that differentiate between the HLA-C subtypes and the present specification teaches only one core serquence of MAGE-A12 (SEQ ID NO: 6) which is specific for Cw*07, but without adequate teaching regarding critical residues within that core sequence. The specification defines a functional variant at page 10, lines 25-32 as "a molecule which contains one or more modifications to the primary amino acid sequence of the MAGE-A12 HLA binding peptide and retains the HLA class I binding properties disclosed herein." Smilek (Proc. Nat. Acad. Sci. (USA) [1991] 88:9633-9637; U1 on form PTO-892) discloses a myelin basic protein peptide with an amino acid change that alters the function of the peptide drastically. Smilek discloses that replacing the lysine at position 4 of the 11-mer with an alanine increases the MHC class II binding of the peptide at least 10 fold, but changes the *in vivo* "function" of the peptide from being encephalogenic to preventative for EAE induction. Accordingly,

greater guidance is required from the specification for the artisan to be able to make and use functional derivatives where amino acid residues are subject to "substitution."

Further, the scope of the claims encompasses the addition or deletion of unspecified amino acid residues to the peptide fragments of SEQ ID NOs: 2. The skilled artisan can make fragments *limited* to *sub*sequences of SEQ ID NO: 2 and encompassing SEQ ID NO: 4, 5, or 6 without undue experimentation. However, before the skilled artisan can make polypeptides comprising with additional flanking amino acid residues that are not part of SEQ ID NO: 2, guidance is required with respect to the identity of those flanking residues. In the instant case however, the specification does not appear to provide this needed guidance. In addition, guidance is required to add intervening amino acid residues within the epitope or to delete intervening amino acid residues within the epitope, as the additional residues or the shortened distance between critical residues would be predicted to interfere with the structure of the epitope. Therefore the scope of the instant claims encompassing functional variants having "amino acid additions" or "amino acid deletions" does not appear to be commensurate with the enablement provided by the instant disclosure.

In view of the breadth of the claims, the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, and the lack of sufficient guidance in the specification, it would take undue trials and errors to make and use the claimed invention.

Conclusion

4. No claim is allowed.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (703) 305-4441. The examiner can normally be reached on M-Th 6:30-4:00; Alternate Fridays 6:30-3:00. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 305-3014.Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

As of January 7, 2004, the Examiner's telephone number will be (571) 272-0852.

F. Pierre VanderVegt, Ph.D.
Patent Examiner
December 15, 2003

PATRICK J. NOLAN, PH.D.
PRIMARY EXAMINER
12/15/03